35 U.S.C. § 112, 1st paragraph

The examiner has rejected claims 1-10 and 16 for "containing subject matter which was not described in the specification" and that the specification "fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation" (office action at 2). Specifically, the examiner contends that "[a]pplicant fails to set forth the criteria for the structure and properties of 'a null IGF-I'" and that "determination of the useful IGF-I...would necessitate an exhaustive search" (office action at 3-4).

However, page 5 describes the properties of null IGF-I, such as "its ability to bind IGFBP-3, but is altered in its receptor binding" (specification at 5, lines 17-31). Moreover, the structural characteristics of various exemplary null IGFs are set forth in the specification: "variants in which one or more of IGF-I's tyrosine residues (*i.e.*, residues 24, 31, or 60) are replaced with non-aromatic residues, (*i.e.*, residues other than tyrosine, phenylalanine or tryptophan), variants where amino acid residues 49, 50, 51, 53, 55 and 56 are altered (for example, where residues 49-50 are altered to Thr-Ser-Ile or where residues 55-56 are altered to Tyr-Gln), and combinations thereof" (specification at 5, lines 27-31). Additionally, at the time of filing, null IGF-I was well defined and examples of null IGF-I have been extensively published. *See* detailed list of publications at 5, lines 23-26. Accordingly, one of ordinary skill would understand which null IGF-I would be useful for the methods claimed in the instant invention.

Furthermore, the examiner has not met her burden of showing that the null IGFs described in the instant invention will not alleviate the symptoms of, or slow the progression of cancer. In other words, the examiner has failed to provide objective indicia supporting her assertion that "the only useful sequence that is shown in the specification is Y60L IGF-I" (office action at 3). The examiner contends that "the specific sites and alterations are too broad" (office action at 3), but this assertion does not substantiate rejecting the pending claims for "non-enablement." "[I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its won with acceptable evidence or reasoning which is inconsistent with the contested statement" (M.P.E.P § 2164.04). Additionally, breadth, per se, is not a proper basis for a lack of enablement rejection. "It is improper to conclude that a disclosure is not enabling based on an analysis of any one of the above [Wands] factors" (M.P.E.P § 2164.01(a)).

Moreover, while Example 2 in the instant application utilizes Y60L IGF-I, as a matter of law, the scope of the claims should not be limited to the working examples. In fact, "[a]n applicant need not have actually reduced the invention to practice prior to filing" (M.P.E.P. § 2164.02, citing *Gould v. Quigg*, 822 F.2d 1074, 1078 (Fed. Cir. 1987) and [t]he specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without undue amount of experimentation" (M.P.E.P § 2164.02, citing In re Borkowski, 422 F.2d 904, 908 (C.C.P.A. 1970).

The examiner also asserts that "the claims are not enabled for alleviating ALL symptoms of ALL cancers" (office action at 4). Applicant has amended claim 1 to more clearly define the present invention. Applicant has found that administration of uncomplexed IGF-I can slow tumor growth more effectively than administration of null IGF-I complexed with IGFBP-3 (*See*, for example, Example 2, and page 6, lines 19-20). This revision should obviate the present rejection.

35 U.S.C. § 112, 2nd paragraph

The examiner has rejected claims 1-10 and 116 for indefiniteness, under 35 U.S.C. § 112, second paragraph. Specifically, the Examiner asserts that "[t]he claims are indefinite regarding the 'null IGF-I' as to the number and positions in the substituted and/or altered sequences" (office action at 4). As discussed *supra*, "null IGF-I" is defined on page 5, lines 17-31 of the specification. At the time of filing, one of ordinary skill would have known what is meant by "null IGF-I." For definiteness, a claim need only reasonably apprise those skilled in the art of the utilization and scope of the invention. *Hybritech, Inc. v. Monoclonal Antibodies,* 231 USPQ 81, 94-95 (1986).

Additionally, the examiner asserts that "[t]he term 'symptoms of cancer' render the claims indefinite" (office action at 4). Specifically, the examiner states that it is allegedly unclear "as to what kind of cancer and which symptoms are intended" by the term "symptoms of cancer" (*Id*). Applicant respectfully disagrees and asserts that the present invention can be used to treat any cancer, but preferably carcinomas. See, for example, page 7, lines 1-2. Nevertheless, claim 1 has been amended so as not to recite "symptoms of cancer." Applicants respectfully urge that the clarifying amendment overcomes the Examiner's rejection for indefiniteness.

Lastly, the examiner also states that the "Sequence Listing compliance is incomplete because" the SEQ ID NOS "have to be entered in all examples and claim(s)" and "the specification cites other sequences that lack a proper SEQ ID NOS"(office action at 5). Upon allowance of the

instant application, applicants will comply with the requirements and amend the application as outlined in the June 8, 2001 communication from the examiner.

Respectfully submitted,

Date 2/19/02

By _____

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. **(Amended)** A method for [alleviating the symptoms of cancer] slowing the growth rate of a tumor, comprising: administering an effective amount of uncomplexed null insulin-like growth factor I (IGF-I) to a subject having cancer[, thereby alleviating the symptoms of the cancer].